QUANTITATIVE VALIDATION OF TOD-BASED TRACTOGRAPHY BY A TRACTOMETER APPROACH

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Introduction: Recently, an extension of the concept of track-density imaging (TDI) that also encodes the *angular* distribution was presented **[1]**. Furthermore, the resulting track orientation distribution (TOD) of a dense full-brain short-tracks tractogram was used as an alternative to the fiber orientation distribution (FOD) from constrained spherical deconvolution (CSD) for the purpose of guiding tractography itself. It was reasoned that the TOD in each voxel has inherent information on the *support of directions by the surroundings* and can therefore guide a track along directions that are more likely to correspond to continuous structure over a longer distance **[1]**. Backed up by this powerful concept, TOD-based tractography was shown to yield promising qualitative results on *in vivo* data of challenging quality. A *quantitative* validation was, however, lacking. In this work, we provide such validation by employing concepts of the recently proposed Tractometer approach **[2]**.

Data: The data consists of an acquisition of the phantom that was also used in **[2]**. The general layout is shown in **Fig.1**. The voxel size equals 3×3×3mm³ (there are 3 slices). We chose to employ the acquisition that provided the overall best results in **[2]**: two repetitions of 64 uniformly distributed DWI-directions at b=1500s/mm².

FOD, TOD-1, TOD-2: FODs were obtained in a "white matter" (WM) region by performing CSD up to a spherical harmonic (SH) order of 8. Outside the WM region, FODs were defined to have zero amplitude. The TODs were constructed as explained in **[1]**; 80 million ***short-tracks*** were generated by probabilistic FOD-based tracking, seeded from the WM region, and using the following parameters: stepsize = 0.2mm, min. radius of curvature = 1mm, min. track length = 24mm, ***max. track length = 48mm***, min. FOD amplitude to initiate/continue tracks = 0.2/0.1. TOD-1 was then obtained by integrating an apodized point spread function of maximum SH order 16 along each track. TOD-2 was obtained in the same way from TOD-1; albeit by setting min. TOD amplitude to initiate/continue tracks = 200000/100000. For further explanation, we refer the reader to **[1]**. In **Fig.2 (*top*)**, FOD, TOD-1 and TOD-2 are compared in a crossing region. Large qualitative improvements are shown.

Tractography: Deterministic as well as probabilistic FOD- and TOD-based tractography was performed using the same (above) parameters; yet without a max. track length, and – specifically for deterministic tracking – without a curvature threshold. MRtrix **[3]** generated tracks until 1000000 were accepted for each experiment. The amount of tracks that had to be generated to achieve this (including rejected tracks) is given in **Tab.1**. "Out of the box", TOD-based tracking produces less tracks that are unable to meet the criteria. A random subset of the deterministic tracks is shown in **Fig.2 (*bottom*)**; qualitative improvements are in line with those in **Fig.2 (*top*)**.

Tractometer: Using the ROIs shown in **Fig.1**, each set of 1000000 tracks was subdivided in *valid connections* (VC), *invalid connections* (IC) and *no connections* (NC); as defined in **[2]**. The percentage of tracks in each of these categories is given in **Tab.2**. For TOD-based tracking, consistent (large) increases of VC and reductions of IC and NC are seen. The additional measure of VC/(VC+IC) reflects the amount of VC one would obtain by enforcing anatomical constraints such as in **[4]** (i.e. tracks *must* connect (gray matter) ROIs, thus NC are absent). In this case, probabilistic TOD-based tracking even scores up to 80%, while its deterministic counterpart has the potential to reach over 90%! As was already reasoned in **[2]**, however, probabilistic methods are surely disadvantaged by the limitations of this particular phantom. The actual VC are shown in **Fig.3**. The TOD-based results provide qualitatively better looking VC; e.g. nicer boundaries and less bulging of bundle 6 into 7, amongst others.

Conclusion: In this work, we provided a much-needed *quantitative* validation of TOD-based tractography. As the Tractometer approach focusses on the connectivity aspect, our results in favour of TOD-based tracking promote its use in the domain of connectomics. Qualitative results, as obtained in **[1]**, are furthermore confirmed.

References: **[1]** Dhollander T. (et al.) Robustifying Probabilistic Tractography by Using Track Orientation Distributions. *Proc. Intl. Soc. Mag. Reson. Med.* 2013;21:774. **[2]** Côté M.A. (et al.) Tractometer: Towards validation of tractography pipelines. *Med. Image Anal.* 2013;17(7):844-857. **[3]** Tournier J.D. (et al.) MRtrix: Diffusion Tractography in Crossing Fiber Regions. *Int. J. Imaging Syst. Technol.* 2012;22(1):53-66. **[4]** Smith, R.E. (et al.) Anatomically-constrained tractography: Improved diffusion MRI streamlines tractography through effective use of anatomical information. *NeuroImage.* 2012;62(3):1924-1938.

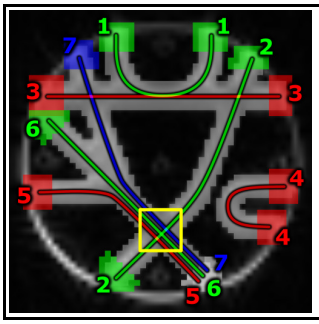

Fig.1: Overview of the phantom, the WM region, ROIs and the seven valid connections between pairs of these ROIs. Note that we delineated all regions ourselves (i.e. they differ from those used in **[2]**). We use the WM region to initially mask the data; yet *not* as a hard stopping criterion for the tractography (the latter is only based on interpolated FOD/TOD amplitudes).

The yellow box indicates the region that is visualized in Fig.2.

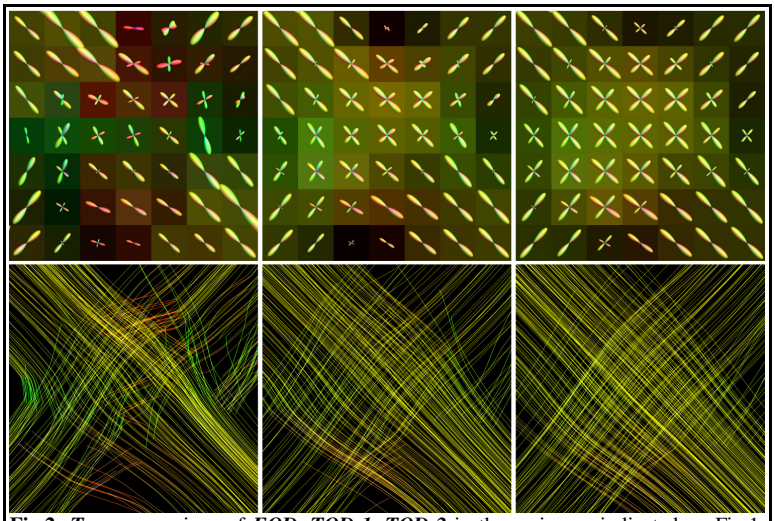

Fig.2: ***Top:*** comparison of ***FOD, TOD-1, TOD-2*** in the region as indicated on Fig.1. ***Bottom:*** sample of (unfiltered) deterministic tracks, guided by ***FOD, TOD-1, TOD-2***.

Tab.1: Amount of tracks that had to be generated by MRtrix **[3]** in order to obtain 1000000 accepted tracks, for each of the 6 tractography experiments.

	FOD	TOD-1	TOD-2
Deterministic	1140993	1001186	1000585
Probabilistic	1104646	1000677	1000212

Tab.2: Tractometer measures indicating the amount of VC, IC, NC and VC/(VC+IC), for each of the 6 sets of 1000000 accepted tracks.

Deterministic			
	FOD	**TOD-1**	**TOD-2**
VC (%)	40.4291	69.1631	75.7147
IC (%)	13.2397	5.8644	4.0825
NC (%)	46.3312	24.9725	20.2028
VC/(VC+IC) (%)	75.3307	92.1837	94.8839
Probabilistic			
	FOD	**TOD-1**	**TOD-2**
VC (%)	29.3934	50.2976	57.8701
IC (%)	13.9695	13.7285	13.3753
NC (%)	56.6371	35.9739	28.7546
VC/(VC+IC) (%)	67.7847	78.5580	81.2264

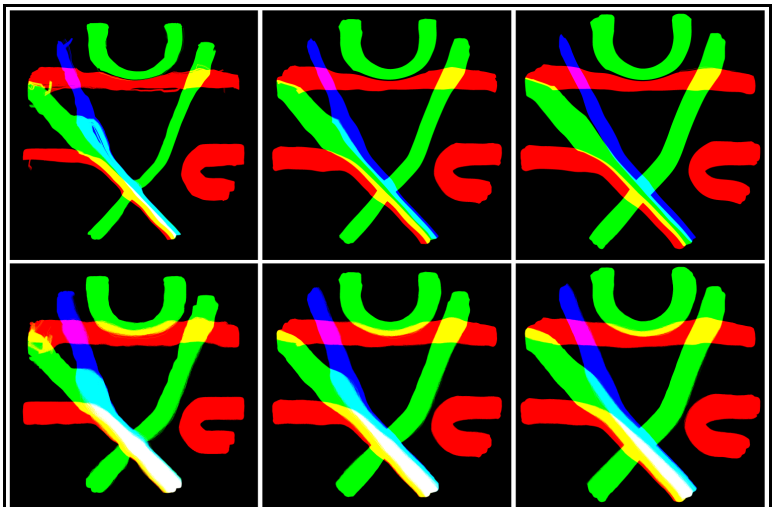

Fig.3: Valid connections (VC), as filtered from the 1000000 deterministic (***top***) and probabilistic (***bottom***) tracks; guided by FOD (***left***), TOD-1 (***middle***), TOD-2 (***right***).